

# Abstract

Prostate specific membrane antigen (PSMA) is a 100 kDa transmembrane protein expressed on prostate cancer cells and the neovasculature of non-prostate solid tumors. We are conducting a phase I clinical trial using repetitively dosed J591, an IgG1 antibody that targets the external domain of PSMA and that can induce antibody-dependent cell-mediated cytotoxicity *in vitro*. The primary endpoint of the study is to determine the toxicities, pharmacokinetic properties, and biodistribution of J591, when used as a vascular targeting agent. Patients are treated in cohorts of three (expandable to six), defined by the following doses: 5, 10, 20, 40, 60, 100 mg of J591. Patients receive one dose every three weeks to a maximum of four doses. Each dose is labeled with 10 mCi of indium-111 as a tracer. Serial serum indium-111 levels, whole body counts, and whole body images are performed to assess pharmacokinetic properties, dosimetry, and tumor localization. NCI Common Toxicity Criteria (version 2) are used to assess toxicities. Standard CT and bone scans are used to evaluate anti-tumor effects, and are performed every six weeks. Three patients with melanoma, three with renal cell carcinoma, and one with breast cancer have been treated to date. Three patients have been treated with 5 mg and four patients have been treated with 10 mg of J591. Median number of cycles was 2 (range 1-4). No grade 4 toxicities were observed. One patient had grade 3 pain secondary to a tumor-related pathologic fracture and one patient had grade 2 transient infusion-related rigors, but otherwise no adverse events are attributable to J591. Indium-111 scans demonstrated localization of antibody to sites involved by tumor by standard imaging. One patient with renal cell carcinoma had stable disease after four cycles. Three patients progressed after 2-4 cycles, one is inevaluable for response, and two patients are currently undergoing treatment. Conclusions: J591 was well tolerated as a vascular targeting agent in this study. It appeared to localize to metastatic melanoma and cancers of the breast and kidney. Pharmacokinetic studies will be analyzed as patients accrue. Significant antitumor effects have not yet been observed. Supported by CaPCURE, the Sacerdote Fund, and PepsiCo.